Remarks

Applicants have canceled claims 1-30 without prejudice to future prosecution and added new claims 330-485. The new claims are directed to a method of selecting for sequences which may be able to distinguish one or more target species from at least one nontarget species, or a method of selecting for sequences which may be able to distinguish two or more target species belonging to a first genus from at least one nontarget species belonging to a second genus. The claims provide the locations where variable regions can be found. As pointed out in the application on page 12, lines 17-19, the sequence evolution at the variable regions (for example, spanning a minimum of 10 nucleotides) is mostly divergent and not convergent.

The application provides figures illustrating where variable regions can be found, provides examples of making and using probes targeted to different variable regions (see Examples 1-18 and 21 at pages 25-95 and 114-118), and at pages 11-12, lines 25-6 points out, with reference to the 16S and 23S rRNA, that:

> These figures also show that the differences are distributed across the entire 16S and 23S rRNA's. Many of the differences, nonetheless, cluster into a few regions. These locations in the rRNA are good candidates for probe design, with our current assay conditions. We also note that the locations of these increased variation densities usually are situated in the same regions of the 16S and 23S rRNA for comparable per cent similarity values. In this manner, we have observed that certain regions of the 16S and 23S rRNA are the most likely sites in which significant variation exists between the target organism and the closest phylogenetic relatives found in a sample.

Thus, the application allows for the design of probes by directing one skilled in the art to variable regions and indicates that such regions once identified are good candidates for designing probes for different organisms or groups of organisms.

The application discusses designing probes to have the appropriate Tm for example, page 9, lines 3 and 4, points out the importance of Tm differences between probe:target duplexes and probe:nontarget duplexes, page 13 describes probe design to achieve the desired Tm differences, and pages 18-20 describe measurement of Tm.

Additional support for screening for probe sequences targeted to different target regions can be found, for example, as follows: original claims 293 and 298 describe methods of producing probes for detecting organisms or groups of organisms by targeting DNA or rRNA, for example, original claim 293 referred to a nucleotide polymer able to distinguish non-viral organisms from at least one nontarget organism or group of nontarget organisms; pages 10-15 describe probe design to variable regions; claims 302, 304, 306, 308, 310, 312, 314, 316, 318, 320, 322, 324, 326 and 328 provide examples of locations of variable regions; support for the region 65-108 *E. coli* 5S rRNA is provided, for example, on page 55, lines 15-19.

The variable regions described in the claims are based on the variable region noted in the claims (as noted in the previous paragraph) and the examples of variable region provided throughout the specification. In some cases, the variable regions noted in the new claims takes into account prior claims (as noted in the previous paragraph) in combination with the descriptions provided in the different examples.

The Examiner previously objected to the title as not being descriptive. The new title is more descriptive of the invention. Reconsideration of this rejection is respectfully requested.

The Examiner previously objected to the claims as not being enabling for failing to provide positive and negative controls. This rejection is respectfully traversed.

The new claims reference particular regions. As discussed above, the application demonstrates that variable regions are clustered together and that such regions are good candidates for probe design. The chose of positive (target) and negative (nontarget) organisms are within the discretion of the person performing the method and depends upon the organism sought to be detected and distinguished therefrom. Preferably, the target and nontarget organisms are phylogenetically very closely related.

The Examiner previously objected to the term "sufficiently complementary to". The new claims do not contain this term.

The Examiner previously objected to the claims as being obvious based on Kohne (U.S. Serial No. 4,851,330). To facilitate allowance of the present application, the claims were amended to indicate where different variable regions can be found. Reconsideration of this rejection is respectfully requested.

The Examiner previously objected to the specification for providing a blank line in page 117. The specification was amended to provide the missing information. Reconsideration of this rejection is respectfully requested.

Accordingly, the claims are now in condition for allowance and a notice to that effect is respectfully requested. If any fee is due in connection with this Amendment, please charge Deposit Account No. 12-2475 for the appropriate amount.

Respectfully submitted,
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